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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Alison A. McCormick

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10/13/2006

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EXAMINER

BLANCHARD, DAVID J

ART UNIT

PAPER NUMBER

1643

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/522,900

Applicant(s)

MCCORMICK ET AL.

Examiner

David J. Blanchard

Art Unit

1643

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 22 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 1-4, 6-23, 29, 37-40 and 54-57.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

  
SHEELA HUFF  
PRIMARY EXAMINER

Continuation of 5. Applicant's reply has overcome the following rejection(s): Applicants' reply filed 9/22/2006 has overcome the rejection of claims 1-4, 6-23, 29, 37-40 and 54-57 under 35 U.S.C. 112, first paragraph, for lack of enablement for a B cell lymphoma "vaccine" in view of the amendments to the claims.

Continuation of 11. does NOT place the application in condition for allowance because:

The rejection of claims 1-4, 6-23, 29, 37-40 and 54-57 under 35 U.S.C. 112, first paragraph because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims is maintained.

The response filed 9/22/2006 argues with certain terms and definitions disclosed in the specification as to what is needed to constitute an idiotypic. This has been fully considered but is not found persuasive. Applicant continues to argue with limitations disclosed but not claimed. The disclosure with which applicant argues states "the polypeptide is preferably a scFv wherein the first domain is the Ig VH domain and the second domain is Ig VL domain, both of which domains create an idiotypic..." (specification at pg. 13, line 21+). Further, applicants' specification indicates that an idiotypic is formed by the association of the hypervariable or complementary determining regions of the VH and VL domains (see page 16 of the specification) and at page 51, lines 7-10, it states: "However, because most idiotypes are expected to be the result of the interaction of the VH with the VL domain, more preferred compositions combine both these regions.", yet the claims remain drawn to a polypeptide self-antigens that only comprise an idiotypic part of a surface immunoglobulin (i.e., short peptide sequence of a surface immunoglobulin), or an epitope of a V region (i.e., part of a CDR or part of a FR), or part of the VH and VL domains (claim 8), or just one CDR (i.e., CDR2), of any two V region domains (i.e., VH-VH pair; claim 7), which encompasses incomplete VH and VL pairs and would not create an idiotypic according to applicant (specification at pg. 13) and the evidence of record. Applicant has not provided any objective evidence that epitopes from a single V region, or from just any two V regions (i.e., VH-VH or VL-VL) or from only part of the VH and VL domains of B-cell lymphoma surface immunoglobulins result in conformational dependent epitopes (idiotypes) mimicking the surface immunoglobulins expressed on B cell lymphomas, that effectively elicits a specific immune response against the B cell lymphomas. Again, Benvenuti et al (cited previously in the Office Action mailed 8/17/04) makes clear that the immune response (i.e., anti-idiotypic antibodies) is directed exclusively against conformationally combined VL/VH determinants (see page 1557, right column), which provides strong evidence that the conformationally combined VH/VL pairs are required to mimic the natural idiotypic of the surface immunoglobulin expressed in B-cell lymphomas. Further, Casper et al (previously cited on PTO-892 mailed 8/17/2004), state: "a change of one or two amino acids in the second complementarity-determining region (CDR2) of the heavy chain seemed to be responsible for the loss of binding to the treatment of MoAb." (anti-idiotypic antibody) (see page 3699, left column). Thus, it is unlikely that epitopes derived from any part of the surface immunoglobulin or epitopes that do not contain both VH and VL domains, would mimic the idiotypes of native surface immunoglobulins expressed in B-cell lymphomas. Again, as stated in the previous office actions, "Applicant is enabled for a scFv idiotypic composition comprising both VH and VL domains obtained from lymphoma cells of a subject, which mimic the natural idiotypic expressed on the surface of B-cell lymphomas." (bottom of pg. 11 of the office action mailed 10/24/2005 and top of pg. 9 of the office action mailed 6/22/2006).

For these reasons and those already of record and incorporated by reference herein, the rejection for lack of enablement is maintained.

The rejection of claims 54 and 56 under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement for introducing new matter is maintained.

The response filed 9/22/2006 has been carefully considered, but is deemed not to be persuasive. Applicant argues that it is the correctly folded nature of the polypeptide that is in part responsible for the polypeptides immunogenicity. This has been fully considered but is not found persuasive. Again, it is reiterated that the disclosure of the polypeptide as being inherently immunogenic so that effective immune responses are generated without the need for fusion to another polypeptide or an adjuvant is with respect to plant expression systems and the inherent immunogenicity of the polypeptide produced thereby. The rejected claims do not require plant expression of the presently claimed polypeptide, which confers the inherent immunogenic properties of the presently claimed polypeptide in the absence of conjugation to another polypeptide. For these reasons and those already of record the rejection for introducing new matter is maintained.

The rejection of claims 1-4, 6-13, 17-23, 29 and 38 under 35 U.S.C 102(b) as being anticipated by Casper et al (Blood, 90(9):3699-3706, November 1997) is maintained.

The response filed 9/22/2006 again argues that the composition of Casper et al is an adenovirus, and not a polypeptide and is not purified, whereas the present claims are drawn to a purified polypeptide. Applicants arguments have been fully considered but are not found persuasive. As stated previously, Casper et al teach a VH-VL scFv fused to GM-CSF, which reads on the presently claimed polypeptide self antigen as "has" is interpreted as equivalent to comprising and is open claim language or inclusive to unrecited elements. Further, Casper et al teach that the scFv-GM-CSF is purified (pg. 3701, 1<sup>st</sup> col.). The examiners reference to the adenovirus of Casper was in response to applicants argument that there is no indication that the scFv of casper in the absence of GM-CSF induces an immune response. Again, as previously acknowledged by applicant, Casper et al teach a scFv (adenovirus) without the GM-CSF, which when expressed in vivo induced an anti-idiotypic immune response, providing evidence that the scFv induces an immune response without the need for adjuvant or other immunostimulatory material (see Figures 2 and 3) (see bridging lines of pages 10-11 of the applicant's response filed 8/2/05). Applicant is reminded that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of anticipation has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). See MPEP 2112 and

2112.01. Applicant has not provided any objective evidence distinguishing the claimed polypeptide self antigen from that of the prior art. For these reasons and those already of record the rejection is maintained.

The rejection of claims 1-4, 6-12, 17-23, 29 and 37-38 under 35 U.S.C 102(b) as being anticipated by Hawkins et al (WO 94/08008, 4/14/1994) is maintained.

The response filed 9/22/2006 argues that Hawkins et al teach immunizing with a nucleic acid and does not teach immunization with the polypeptide functions to elicit the claimed immune response. It is reiterated that Hawkins et al teach a scFv that is an idiotypic determinant (i.e., epitope) of an immunoglobulin expressed on the surface of a B cell lymphoma and the scFv is purified and administration of the scFv generated an anti-idiotypic response, clearly indicating that the scFv was in correctly folded form and mimicked the idio type of the immunoglobulin expressed on the B cell lymphomas (see pages 19-21). Further, as above, Applicant is reminded that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). See MPEP 2112 and 2112.01. Applicant has not provided any objective evidence distinguishing the claimed polypeptide self antigen from that of the prior art. For these reasons and those already of record the rejection is maintained.

The rejection of claims 1-4, 6-23, 29, 37-40, 54-55 and applied to newly added claim 57 under 35 U.S.C. 103(a) as being unpatentable over Caspar et al (Blood, 90(9):3699-3706, November 1997) in view of Fiedler et al (Immunotechnology, 3(3):205-216, October 1997, lds filed 3/8/04) and Tang et al (Journal of Biological Chemistry, 271(26):15682-15686, June 1996) and Hakim et al (Journal of Immunology, 157:5503-5511, 1996) is maintained.

The response filed 9/22/2006 appears to argue as above against Casper et al and the examiners comments above apply here as well. The remainder of applicants remarks question the operability of the prior art teachings and applicant argues that there would not be a reasonable expectation of success in producing the claimed polypeptide self antigen effective for tumor therapy. Applicant is reminded that obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). Again, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Additionally, the use of the randomized linkers of Tang et al for the production of scFvs in the plant expression system of Fiedler et al would necessarily produce scFvs that elicit an appropriate immune response. Again, in view of the combined teachings of Casper et al and Fiedler et al and Tang et al and Hakim et al, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have produced a scFv idio type composition comprising an adjuvant, IL-2 or IFN-gamma wherein the VH and VL domains are obtained from lymphoma cells of a subject, linked by a randomized linker and produced using a plant expression system, which is identical to the presently claimed scFv idio type composition (inclusive to an adjuvant such as IL-2 or IFN-gamma, particularly in view of claims 37-39) wherein the VH and VL domains are obtained from lymphoma cells of a subject, linked by a randomized linker and produced using a plant expression system. Therefore, it is the Examiner's position that Casper et al and Fiedler et al and Tang et al and Hakim et al have produced idio type-bearing scFvs that are identical to the claimed idio type-bearing scFvs. One of ordinary skill in the art would reasonably conclude that the idio type-bearing scFvs of Casper et al and Fiedler et al and Tang et al and Hakim et al also possesses the same structural and functional properties as those of the idio type-bearing scFvs claimed and, therefore, it appears that Casper et al and Fiedler et al and Tang et al and Hakim et al have produced idio type-bearing scFvs that are identical to the claimed idio type-bearing scFvs. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed idio type-bearing scFvs with the idio type-bearing scFvs of Casper et al and Fiedler et al and Tang et al and Hakim et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed idio type-bearing scFvs and the idio type-bearing scFvs of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). See MPEP 2112 and also MPEP 716.01 (i.e., unexpected properties, inoperability of the prior art).

Respectfully,  
David J. Blanchard  
571-272-0827

